

## Reconstruction of proto-vertebrate, proto-cyclostome and proto-gnathostome genomes provides new insights into early vertebrate evolution

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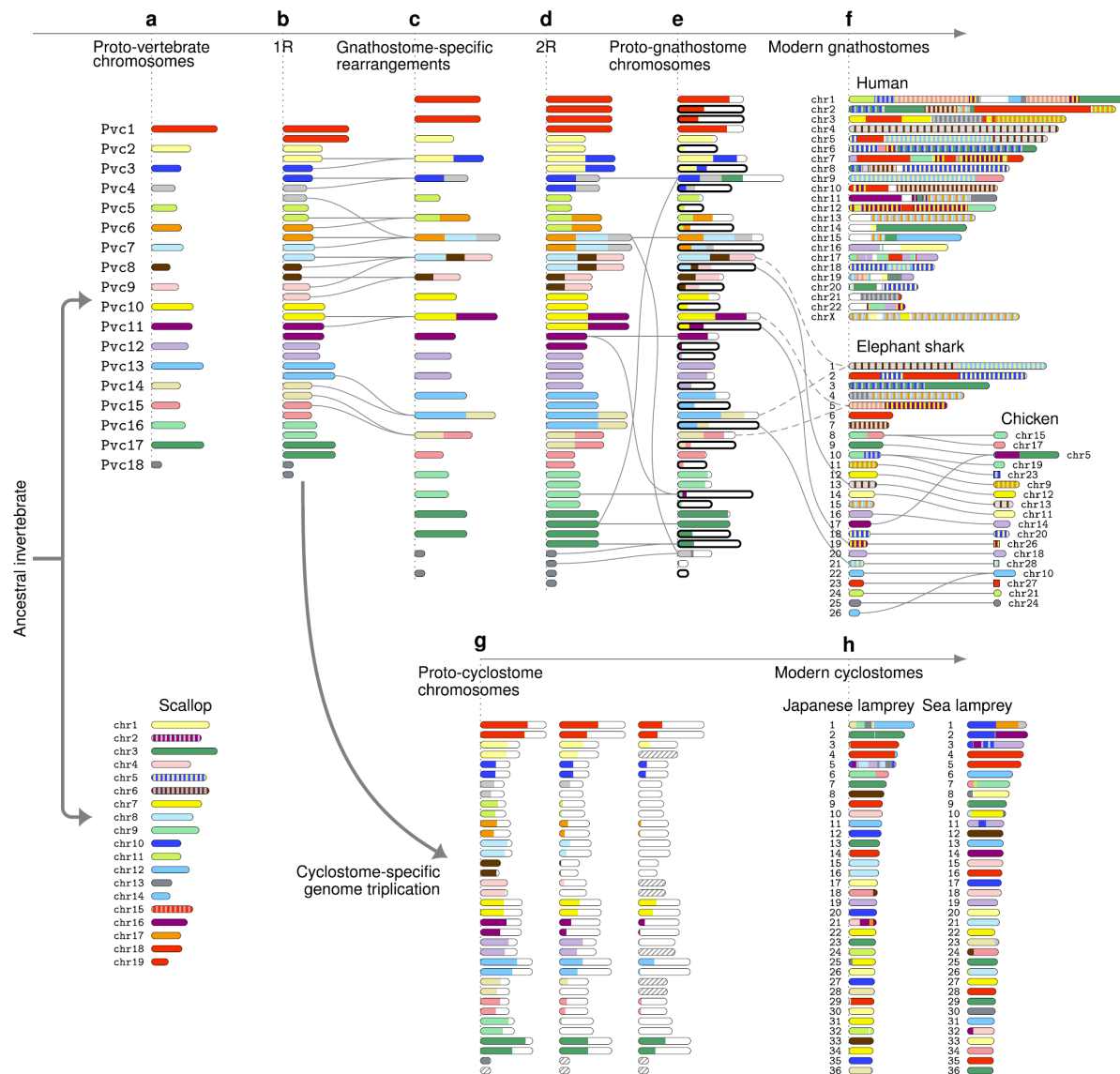
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## **Abstract**

Ancient polyploidization events have had a lasting impact on vertebrate genome structure, organization and function. Some key questions regarding the number of ancient polyploidization events and their timing in relation to the cyclostome-gnathostome divergence have remained contentious. Here we generate de novo long-read-based chromosome-scale genome assemblies for the Japanese lamprey and elephant shark. Using these and other representative genomes and developing algorithms for the probabilistic macrosynteny model, we reconstruct high-resolution proto-vertebrate, proto-cyclostome and proto-gnathostome genomes. Our reconstructions resolve key questions regarding the early evolutionary history of vertebrates. First, cyclostomes diverged from the lineage leading to gnathostomes after a shared tetraploidization (1R) but before a gnathostome-specific tetraploidization (2R). Second, the cyclostome lineage experienced an additional hexaploidization. Third, 2R in the gnathostome lineage was an allotetraploidization event, and biased gene loss from one of the subgenomes shaped the gnathostome genome by giving rise to remarkably conserved microchromosomes. Thus, our reconstructions reveal the major evolutionary events and offer new insights into the origin and evolution of vertebrate genomes.

**Figure**



**Figure Legend:** Our reconstruction of the ancestral vertebrate genomes shows that the ancestor of all vertebrates (the proto-vertebrate) comprised 18 chromosomes, which are conserved in several basal invertebrates such as scallop (a) and *Trichoplax*. The proto-vertebrate genome underwent one whole-genome duplication, the so called 1R (b) after which the lineages of the jawed vertebrates (gnathostomes) and jawless vertebrates (cyclostomes) separated. Subsequently the gnathostome ancestor experienced nine chromosomal fusions

(c) followed by a second round of whole-genome duplication, the so called 2R (d). The cyclostome ancestor on the other hand underwent triplication of the genome (g) which explains the approximately 100 chromosomes in the present-day lampreys. Our model provides a new framework for understanding the genetic bases of the differences in the phenotype of jawless and jawed vertebrates such as the highly complex but divergent adaptive immune systems of the two.

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